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<p><i>Salmonella, Shigella, and Yersinia</i> cause a well-characterized spectrum of disease in humans, ranging from asymptomatic carriage to hemorrhagic colitis and fatal typhoidal fever. These pathogens are responsible for millions of cases of food-borne illness in the United States each year, with substantial costs measured in hospitalizations and lost productivity. In the developing world, illness caused by these pathogens is not only more prevalent but also associated with a greater case-fatality rate. Classic methods for identification rely on selective media and serology, but newer methods based on mass spectrometry and polymerase chain reaction show great promise for routine clinical testing.</p>	
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<p>Shiga toxin-producing <i>Escherichia coli</i> (STEC) is among the common causes of foodborne gastroenteritis. STEC is defined by the production of specific toxins, but within this pathotype there is a diverse group of organisms. This diversity has important consequences for understanding the pathogenesis of the organism, as well as for selecting the optimum strategy for diagnostic testing in the clinical laboratory. This review includes discussions of the mechanisms of pathogenesis, the range of manifestations of infection, and the several different methods of laboratory detection of Shiga toxin-producing <i>E. coli</i>.</p>	
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<p>Vibriosis is a group of intestinal and extraintestinal infections caused by marine-dwelling bacteria of the genus <i>Vibrio</i>. Infections range from indolent illnesses to fulminant diseases, including cholera and necrotizing fasciitis. Most illnesses result from direct contact with the marine environment or consumption of shellfish, especially oysters. In the United States vibrio infections are increasing but are underreported because of lack of clinical recognition and appropriate detection in the microbiology laboratory. Recent advances to aid in the detection and identification of vibrio illnesses in the laboratory include rapid identification tests, new media, and molecular identification systems.</p>	

Campylobacter

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Collette Fitzgerald

Campylobacter continues to be one of the most common bacterial causes of diarrheal illness in the United States and worldwide. Infection with *Campylobacter* causes a spectrum of diseases including acute enteritis, extraintestinal infections, and postinfectious complications. The most common species of *Campylobacter* associated with human illness is *Campylobacter jejuni*, but other *Campylobacter* species can also cause human infections. This comprehensive review includes discussion of the taxonomy, clinical manifestations of infection, epidemiology and the different methods of laboratory detection of *Campylobacter*.

Optimizing the Laboratory Diagnosis of *Clostridium difficile* Infection

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Peter H. Gilligan

The best laboratory diagnostic approach to detect *Clostridium difficile* infection (CDI) is the subject of ongoing debate. In the United States, nucleic acid amplification tests (NAAT) have become the most widely used tests for making this diagnosis. Detection of toxin in stool may be a better predictor of CDI disease and severity. Laboratories that have switched from toxin-based to NAAT-based methods have significantly higher CDI detection rates. The important issue is whether all NAAT-positive patients have CDI or at least some of those patients are excretors of the organism and do not have clinical disease.

Antimicrobial Susceptibility Testing of Bacteria That Cause Gastroenteritis

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Romney M. Humphries and Audrey N. Schuetz

Gastroenteritis due to enteric pathogens is generally a self-limiting disease for which antimicrobial treatment is not required. However, treatment should be considered for cases of severe or prolonged diarrhea, extraintestinal isolation of bacteria, or diarrhea in immunocompromised hosts, the elderly, and infants. Various resistance trends and current issues concerning antimicrobial susceptibility testing of enteric pathogens are reviewed in this article, including *Campylobacter*, *Salmonella*, *Shigella*, *Vibrio*, *Aeromonas*, *Plesiomonas*, and *Clostridium difficile*. Updated interpretive criteria from breakpoint-setting organizations are reviewed, along with explanations for recent changes in antimicrobial breakpoints.

Markers of Intestinal Inflammation for the Diagnosis of Infectious Gastroenteritis

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Mark D. Gonzalez, Craig B. Wilen, and Carey-Ann D. Burnham

Infectious diarrhea is a major cause of morbidity. A rapid and inexpensive assay for the diagnosis of infectious gastroenteritis would expedite appropriate therapy and prevent unnecessary and potentially invasive testing. This article summarizes assays for the diagnosis of infectious gastroenteritis based on the host response to bacterial, viral, or parasitic infection. This includes both systemic biomarkers (such as C-reactive protein, erythrocyte sedimentation rate, and serum cytokines) and fecal biomarkers (such as lactoferrin, fecal leukocyte analysis, and calprotectin). Although some of these assays have value as adjunct diagnostics, they lack sensitivity and specificity as stand-alone tests in this setting.

Laboratory Diagnosis of Noroviruses: Present and Future 345

Xiaoli Pang and Bonita E. Lee

Norovirus is an important cause of gastroenteritis outbreaks globally and the most prevalent cause of sporadic gastroenteritis in many regions. Rapid and accurate identification of causative viral agents is critical for outbreak investigation, disease surveillance, and management. Because norovirus is not cultivable and has a highly diversified and variable genome, it is difficult to develop diagnostic assays. Detection methods have evolved from electron microscopy to conventional end-point reverse transcription polymerase chain reaction (RT-PCR), immunoassay, real-time RT-PCR, other molecular technologies, and nanotechnology array-based assays. The status and features of various testing methods are summarized in this review.

Rotavirus 363

Mathew D. Esona and Rashi Gautam

Group A rotavirus (RVA) is the major cause of acute gastroenteritis (AGE) in young children worldwide. Introduction of two live, attenuated rotavirus vaccines, Rotarix® and RotaTeq®, has dramatically reduced RVA-associated AGE and mortality. High-throughput, sensitive and specific techniques are required to rapidly diagnose and characterize rotavirus strains in stool samples for proper patient treatment and to monitor circulating vaccine and wild-type rotavirus strains. New molecular assays are rapidly developed that are more sensitive and specific than the conventional assays for detection, genotyping and full genome characterization of circulating rotavirus wild-type and vaccine (Rotarix® and RotaTeq®) strains causing AGE.

Intestinal Amebae 393

Ibne Karim M. Ali

Among the *Entamoeba* species that infect humans, *Entamoeba histolytica* causes diseases, *Entamoeba dispar* is a harmless commensal, *Entamoeba moshkovskii* seems to be a pathogen, and the pathogenicity of *Entamoeba bangladeshi* remains to be investigated. Species-specific detection needed for treatment decisions and for understanding the epidemiology and pathogenicity of these amebae. Antigen-based detection methods are needed for *E. dispar*, *E. moshkovskii*, and *E. bangladeshi*; and molecular diagnostic test capable of detecting *E. histolytica*, *E. dispar*, *E. moshkovskii*, and *E. bangladeshi* simultaneously in clinical samples. Next-generation sequencing of DNA from stool is needed to identify novel species of *Entamoeba*.

Infections by Intestinal Coccidia and *Giardia duodenalis* 423

Vitaliano A. Cama and Blaine A. Mathison

The coccidians *Cryptosporidium* spp, *Cyclospora cayetanensis*, and *Cystoisospora belli* and the flagellate *Giardia duodenalis* are pathogenic protozoa associated with gastrointestinal manifestations. Diagnosis relies heavily on microscopy, and although ova-and-parasite examinations can detect *Giardia* and *Cystoisospora*, *Cryptosporidium* and *Cyclospora* often

require specific diagnostic requests. Approved non-microscopy methods are available for *Giardia* and *Cryptosporidium*, although negative results are frequently followed by microscopic assays. Polymerase chain reaction-based methods are not frequently used for diagnosis of *Giardia* and *Cryptosporidium* and have been used primarily for epidemiologic or outbreak investigations of *Giardia* and *Cryptosporidium*.

Intestinal Microsporidiosis

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Andrew S. Field and Danny A. Milner Jr

Infection by the ingested pathogens of microsporidia occur primarily in immunosuppressed patients (including untreated HIV/AIDS) and are diagnosed by stool examination, small bowel biopsy with special stains, or electron microscopy (for definitive speciation), or by various molecular techniques. Although electron microscopy has been the definitive diagnostic tool for speciation, genetic sequencing increasingly provides the definitive diagnosis for new species, such as *Anncaliia algerae*. Further genetic sequencing of the common pathogens may allow for the development of advanced molecular diagnostics providing high diagnostic sensitivity and throughput.

Multiplex Polymerase Chain Reaction Tests for Detection of Pathogens Associated with Gastroenteritis

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Hongwei Zhang, Scott Morrison, and Yi-Wei Tang

A wide range of enteric pathogens can cause infectious gastroenteritis. Conventional diagnostic algorithms are time-consuming and often lack sensitivity and specificity. Advances in molecular technology have provided new clinical diagnostic tools. Multiplex polymerase chain reaction (PCR)-based testing has been used in gastroenterology diagnostics in recent years. This article presents a review of recent laboratory-developed multiplex PCR tests and current commercial multiplex gastrointestinal pathogen tests. It focuses on two commercial syndromic multiplex tests: Luminex xTAG Gastrointestinal Pathogen Panel and BioFire FilmArray gastrointestinal test. Multiplex PCR tests have shown superior sensitivity to conventional methods for detection of most pathogens.